Histone H3.3 regulates dynamic chromatin states during spermatogenesis.

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Public Summary:
The histone variant H3.3 is involved in diverse biological processes, including development, transcriptional memory and transcriptional reprogramming, as well as diseases, including most notably malignant brain tumors. Recently, we developed a knockout mouse model for the H3f3b gene, one of two genes encoding H3.3. Here, we show that targeted disruption of H3f3b results in a number of phenotypic abnormalities, including a reduction in H3.3 histone levels, leading to male infertility, as well as abnormal sperm and testes morphology. Additionally, null germ cell populations at specific stages in spermatogenesis, in particular spermatocytes and spermatogonia, exhibited increased rates of apoptosis. Disruption of H3f3b also altered histone post-translational modifications and gene expression in the testes, with the most prominent changes occurring at genes involved in spermatogenesis. Finally, H3f3b null testes also exhibited abnormal germ cell chromatin reorganization and reduced protamine incorporation. Taken together, our studies indicate a major role for H3.3 in spermatogenesis through regulation of chromatin dynamics

Scientific Abstract:
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